In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Case No. 08-864V

Filed: April 18, 2016

[TO BE PUBLISHED]

LISA SMITH,	*	
	*	
	*	
Petitioner,	*	Hepatitis B Vaccine; Multiple Sclerosis;
	*	Myelin Oligodendrocyte ("MOG") Protein;
v.	*	Molecular Mimicry.
	*	
SECRETARY OF HEALTH	*	
AND HUMAN SERVICES,	*	
	*	
Respondent.	*	

Michael G. McLaren, Black McLaren, PC, Memphis, TN, for petitioner.
Lara A. Englund, United States Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

Gowen, Special Master:

On December 4, 2008, Lisa Smith ("petitioner" or "Ms. Smith") filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10 – 34 (2012)[2] (the "Vaccine Act" or "the Program"). Petitioner alleged that as a result of

[1] Because this published ruling contains a reasoned explanation for the action in this case, I intend to post it on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to delete medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will delete such material from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

receiving a Hepatitis B (or "Hep B") vaccine on December 20, 2005, she developed multiple sclerosis (or "MS"), optic neuritis, and other injuries which persisted for over six months. Petition at ¶ 2, 3, docket no. 1, filed Dec. 4, 2008. An entitlement hearing was held in Charlotte, North Carolina on February 3 and 4, 2015. Based on the evidence and testimony presented, I find that petitioner is entitled to compensation.

I. BACKGROUND

A. Procedural History

This case was assigned to Special Master Abell in December 2008, when the petition was filed. On February 27, 2009, petitioner filed an affidavit and several medical records in support of her petition. *See* Petitioner's Exhibit ("Pet. Ex.") 1-11, docket no. 5, filed Feb. 27, 2009. An initial status conference was held on April 14, 2009, after which petitioner was ordered to file additional medical records and fact witness affidavits. *See* Order, docket no. 9, filed Apr. 21, 2009. Petitioner filed additional medical records, affidavits, and a letter from her treating physician, Dr. Haque, as exhibits 14 through 34.

A telephonic status conference was held on May 3, 2011 to discuss whether a fact hearing to establish the facts of petitioner's case was appropriate. Thereafter, a fact hearing was scheduled for November 15, 2011. *See* Order, docket no. 42, filed June 8, 2011. A prehearing status conference was held on October 4, 2011, where it was decided that petitioner herself would testify at the fact hearing. *See* Order, docket no. 45, filed Oct. 4, 2011.

The fact hearing proceeded as scheduled on November 15, 2011, in Raleigh, North Carolina. Petitioner was the only testifying witness. Ms. Smith presented testimony on the events surrounding the series of Hep B vaccinations she received, how her alleged vaccine injury developed, and her then-present state of health. *See* Fact Transcript ("Fact Tr."), docket no. 48, filed Dec. 16, 2011.

Thereafter, on December 20, 2011, petitioner was ordered to file an expert report. *See* Order, docket no. 49, filed Dec. 20, 2011. On December 22, 2011, petitioner filed as exhibit 35, her personnel file from Randolph Hospital, where she was employed, and filed MRI images on CD as exhibits 36 to 39 on December 27, 2011. On October 17, 2012, petitioner filed medical records from Orthopaedic Surgery Center as exhibit 40. Petitioner later filed medical records from Horizon Internal Medicine and Randolph Hospital as exhibits 41 and 42.

On July 22, 2013, petitioner filed an expert report, curriculum vitae, and medical literature from Dr. Lawrence Steinman. *See* Pet. Exs. 43-57, docket no. 62, filed Jul. 22, 2013. Respondent was then ordered to file a responsive expert report and Rule 4 Report. On November 15, 2013, respondent filed a Rule 4 Report, expert report, curriculum vitae, and medical literature from Dr. David Alexander. *See* Respondent's Exhibit ("Res. Ex.") A-B, docket no. 37, filed Nov. 15, 2013.

The parties were then ordered to provide dates for an entitlement hearing and respondent was ordered to file a status report identifying contested issues of fact arising from the fact

hearing held on November 15, 2011. *See* Scheduling Order, docket no. 70, filed Jan. 29, 2014. Thereafter, an entitlement hearing was scheduled for February 3 and 4, 2015 in Charlotte, North Carolina. Prior to that hearing, this case was assigned to me on September 4, 2014. Petitioner filed prehearing submissions on November 10, 2014, and respondent filed prehearing submissions on December 12, 2014.

At the entitlement hearing, Ms. Smith and her daughter, Kaitlyn Tedder, testified. Additionally, Dr. Steinman testified on behalf of petitioner, and Dr. Alexander testified on behalf of respondent. Petitioner filed a post-hearing brief on May 1, 2015 and respondent filed a post-hearing brief on June 4, 2015. Petitioner filed a reply to respondent's post hearing brief on June 29, 2015.

This matter is now ripe for a decision on entitlement.

B. Summary of the Facts

Petitioner was thirty-four years old when she received the Hepatitis B vaccination at issue here. This was her third Hepatitis B vaccination and was received on December 20, 2005.

1. Medical History Prior to Vaccination

Petitioner's medical history is significant for treatment for weight loss, depression, anxiety, scoliosis, chronic back pain, suspicion of a pituitary tumor resulting in galactorrhea, a motor vehicle accident in 1994, and another in June 2003 when she was four months pregnant. She was seen in the emergency room after the latter motor vehicle accident for low back pain, abdominal pain, and left hip pain. *See generally* Pet. Exs. 3, 26, 27. An MRI of the pituitary gland on January 20, 2007 showed no evidence of a pituitary tumor. Pet. Ex. 7 at 51.

When she was nine months pregnant on December 5, 2003 she was admitted to the hospital with severe low back pain. She was seen by Stephen Ford M.D. Dr. Ford, a board certified neurologist, noted that he had treated petitioner for back pain since September 22, 2003, and that she had longstanding back pain "since at least 1994" which was managed by Dr. Greg Mieden, another neurologist in Dr. Ford's office. Pet. Ex. 4 at 62. Dr. Ford noted that "in the past, [petitioner's] back pain ha[d] always been primarily in the interscapular region," but then she developed "a lot of low back pain," and also "occasional neck pain which [was] not nearly as troublesome as the interscapular pain or the lumbar pain." *Id.* Dr. Ford also noted that petitioner had intermittent problems with numbness and tingling in her arms and legs. *Id.* On this occasion, he noted that the prior night the pain had become so severe that she could not get in or out of bed and needed assistance with dressing. *Id.* It also changed in character. *Id.* It was in the lumbar spine, worse on the left, and radiating into her left buttock and into her left medial thigh. *Id.* She denied pain below the knee and denied any numbness in her legs. *Id.* He noted that there had not been an accident or trauma to explain the acute pain. *Id.* Dr. Ford discussed an epidural injection or continued treatment with Vicodin. *Id.* Ms. Smith elected to treat with Vicodin given that she was thirty-eight weeks pregnant. *Id.* Her pain had subsided sufficiently by the day after admission, when Dr. Ford saw her, that she was able to be discharged home. *Id.* A week later she gave birth to a son on December 10, 2003. The delivery notes indicated left leg

paresthesia but the delivery was uncomplicated. *See* Pet. Ex. 4 at 18. Petitioner was discharged home on December 12, 2003. *Id.*

On February 19, 2004, Dr. Ford ordered MRIs of the cervical, thoracic and lumbar spine. Pet. Ex. 5 at 7-9. A sagittal MRI view showed small disc protrusions at C5-6 and C6-7. *Id.* at 9. The lumbar spine MRI showed minimal degenerative disc disease and a small disc bulge with a possible tear of the L4-5 disc. *Id.* at 8. There was no nerve impingement. *Id.* The thoracic spine MRI showed "two very tiny disc bulges" with no nerve impingement. *Id.* at 9. There were no plaques or spinal cord lesions identified on any of these MRI scans.

On February 24, 2004, Ms. Smith visited a physical therapist, Dr. Hassan, at Randolph Hospital for thoracic back pain. Pet. Ex. 3 at 10. It was noted that the onset of the back pain was June 17, 2003 after a motor vehicle accident when she was pregnant, and that she had a history of upper and low back pain, scoliosis, bulging discs and degenerative disc disease. *Id.* The record also noted numbness in her right foot and sometimes in her arms when holding her baby, as well as pain in her left leg. *Id.* at 11. The plan of treatment was to see petitioner for modalities and physical therapy as needed, along with strengthening, condition, and flexibility exercises three times a week for four weeks. *Id.* at 14.

On June 1, 2004, petitioner presented to the emergency department for low back pain radiating into the left leg, which began a week prior. Pet. Ex. 3 at 25. Dr. Kim Lykins examined her and took a history in the emergency room. He noted a history of chronic low back pain which was getting worse. *Id.* The pain radiated down her left leg to her foot. *Id.* She felt that lifting a seventeen pound baby might have aggravated her condition. *Id.* She had no urinary tract, bladder or bowel symptoms. *Id.* He noted that she had a prior motor vehicle accident in June 2003 that caused a back injury. *Id.* She reported no numbness or tingling. *Id.* In the section of the note denominated "Physical Examination" next to "Neurological" he noted, "There is decreased Achilles on the left. *She reports* decreased sensation in her entire left leg. Heel-toe intact. There is positive [sic] for equivocal straight leg raising on the left." *Id.* (emphasis added). Under "Back" the note said "she has pain at the left lumbosacral junction. She has pain with any motion at all, so it is very difficult for her to rise. She cannot stand up erect." *Id.*

Petitioner underwent physical therapy for weakness, range of motion limitation, functional skills impairment, and back pain in 2004. Pet. Ex. 3 at 16. Physical therapy records from June 24, 2004 noted that she experienced numbness in her right foot and sometimes in her arms when holding her baby. *Id.* at 11. Additionally, petitioner experience pain in her left leg. *Id.*

On May 11, 2005, petitioner visited her primary care doctor, Dr. Imran Haque, for upper back and bilateral shoulder pain. Pet. Ex. 27 at 4. Petitioner reported no significant trauma or exercise which might have induced the pain. *Id.* She reported that the pain suddenly came on and had lasted for several days. *Id.* Dr. Haque prescribed Flexeril for muscle relaxation and Tylenol for pain relief. *Id.*

On June 13, 2005, petitioner received the first dose of Hepatitis B vaccine as a new employee at Randolph Hospital. *See* Pet. Ex. 13 at 8; Entitlement Transcript ("Tr.") at 10.

Petitioner testified that she felt a "bit of dizziness" for approximately two days after this vaccination; however she did not experience any other issues. Tr. at 10. Petitioner received her second dose of Hepatitis B vaccine on July 15, 2005. Pet. Ex. 13 at 8. Petitioner testified that after this vaccination she experienced dizziness and saw dots. Tr. at 10. This lasted for approximately two weeks and subsided. *Id.* at 11. On December 20, 2005, petitioner received the last dose of Hepatitis B vaccine, which is at issue here.[3] Pet. Ex. 13 at 8. She testified that she felt dizzy in the moments after this vaccination, and that she stayed in a dark room to rest for a little while before returning to work. Tr. at 13-14.

Ms. Smith testified that in August 2005, while at Randolph Hospital where she worked, she moved her department off-site to a satellite office. She said that she was the happiest she had even been at that time, was enjoying her job and was in good health. Tr. at 11-12, 33. She described carrying a seventy-five pound printer down the street to the new office without any problems. *Id.* at 11-12. Nothing was wrong with her back. *Id.* at 12. Her daughter also described the normality of the family's Thanksgiving activities in 2005. As discussed below, her daughter explained that her mother participated in all of the family activities and had no appearance of health problems. *Id.* at 53-54.

2. Medical History After the Third Hepatitis B Vaccination

A few days after the December 20th Hepatitis B vaccination, on December 25, 2005, petitioner experienced visual disturbance and dizziness while showering in the morning. Tr. at 15. She lay down to rest for much of the day, and could participate in her family Christmas traditions only late in the afternoon. *Id.* at 15. While driving back home from her mother's house that evening, petitioner experienced double vision, where it seemed the headlights of the car in the opposite lane were coming toward her. *Id.* at 17. Petitioner testified that due to fatigue for much of the day, she was unable to wrap presents for her children. *Id.* at 16. According to petitioner, this time her symptoms persisted and included severe neck pain and blurry vision that became worse and continued after the children returned to school and after she returned to work in January. *Id.* at 16-17. At the time she thought that the neck pain might be caused by working at a call desk without the use of a headset. *Id.* at 33.

Petitioner underwent lab testing on January 8, 2006, which revealed a value for Hepatitis B antibodies of greater than 2000, well above the reference range of 0.0 to 8.9. Pet. Ex. 3 at 48. On February 15, 2006, petitioner visited Dr. Haque for a routine check-up and follow up for increased stress. Pet. Ex. 27 at 8-9. She reported that she was depressed and experiencing crying spells. Dr. Haque prescribed Xanax for possible anxiety. *Id.* at 7. Petitioner returned to Dr. Haque the following day for increased stress, depression, anxiety, and new onset of heart

[3] A vaccine injury attributable to petitioner's first two Hepatitis B vaccinations are not compensable, as a petition for those claims would have been filed out of time. Petitioner filed a petition on December 4, 2008. The onset of symptoms related to the first Hepatitis B vaccination allegedly occurred on June 13, 2005, and the onset of symptoms related to the second Hepatitis B vaccination allegedly occurred on July 15, 2005. Nevertheless, these symptoms were transient and appeared to resolve completely.

palpitations. *Id.* at 8. He increased her dose of Xanax and awaited results of her lab work. *Id.* In a follow up appointment on February 22, 2006, petitioner reported the onset of flu symptoms, including body aches, a sore throat, and a fever. *Id.* at 10. Petitioner also reported a ten pound weight gain over the previous week. *Id.* Petitioner was started on Tamiflu. *Id.* She described that during the early months of 2006, her pain became so bad that she was driving the kids to school with her head leaning on the window of the car. Tr. at 42.

In April 2006, petitioner was evaluated at an urgent care center by Dr. Robert Brown for dizziness, occasional blurred vision, fatigue, and galactorrhea for three months. Pet. Ex. 3 at 50. Dr. Brown ordered a brain MRI, which was performed on May 1, 2006. The MRI revealed a 0.8 enhancing lesion in the right temporal white matter. *Id.* at 54. The impression was the lesion was non-specific. *Id.* The MRI also revealed chronic mild flattening of her pituitary gland, which was suggestive of a pituitary tumor. *Id.*

Petitioner visited her primary care doctor, Dr. Haque, on September 13, 2006 for low back pain radiating to the lower legs. Pet. Ex. 12 at 2. Petitioner reported that the pain began when she almost fell to the floor at work while attempting to sit in a chair. *Id.* She reported no numbness or tingling of the lower extremities. *Id.* Petitioner also developed neck and right shoulder pain after the near fall. *Id.* Dr. Haque prescribed Oxycodone, Skelaxin, and Celebrex. *Id.*

On September 19, 2006, petitioner visited Dr. Keung Lee for her neck and right shoulder pain, which radiated to her right arm. Pet. Ex. 26 at 2. Dr. Lee gave petitioner an injection of Kenalog mixed with Lidocaine in her right shoulder. *Id.* He also prescribed Prednisone, Relafen, Norflex and a Lidoderm patch. *Id.* A few days later, petitioner visited endocrinologist, Dr. Roger Smith. *See* Pet. Ex. 18 at 9. Dr. Smith increased her dose of Dostinex and ordered lab tests. *Id.*

Petitioner returned to Dr. Lee on October 3, 2006 to manage her chronic back pain. Petitioner reported improvement of her back pain, but she still experienced frequent muscle tension. Pet. Ex. 26 at 4. Petitioner also reported that she experienced double vision after a cortisone injection she received at a previous appointment on September 26, 2006. *Id.* Dr. Lee noted that petitioner had a standing appointment to visit an endocrinologist and ophthalmologist. *Id.* Dr. Lee decided not to give any more cortisone injections and continued her treatment with Relafen, Vicodin, and a Lidoderm patch. *Id.* He also noted that he awaited workman's compensation approval for petitioner to undergo physical therapy. *Id.*

Petitioner had an eye exam on October 4, 2006 where it was noted that by her history she had a pituitary tumor and diabetes. Pet. Ex. 16 at 1. The ophthalmologist also noted petitioner's ongoing problem with nighttime driving, double vision, and blurred vision. *Id.* at 1, 3. Her unaided eye sight was 20/30 in both eyes. *Id.* at 2. She was diagnosed with hyperopia and astigmatism and a follow-up appointment in six months was recommended. *Id.* at 1; tr. at 139.

Petitioner continued treatment with Dr. Lee, Dr. Smith, Dr. Haque, and a physical therapist through August 2007 for her right shoulder and neck pain, right shoulder bursitis and tendinitis, and hyperprolactinemia. *See* Pet. Exs. 3 at 34-42, 62-65; 18 at 7-8; 12 at 4-5; 26 at 1,

6. In August 2007, petitioner reported increased numbness in both arms with rightward neck rotation. Pet. Ex. 3 at 38. She also reported lip numbness the night before her physical therapy appointment on August 23, 2007. Pet. Ex. 3 at 45.

On September 13, 2007, petitioner visited neurologist Dr. Elaine Feraru for a follow up appointment. Petitioner reported numbness and tingling radiating down her arm to the second and third fingers, and pain in her right shoulder. Pet. Ex. 7 at 22. Petitioner also reported symptoms of diplopia for about a month, numbness in the left side of her face associated with her neck pain, and mid-back pain. *Id.* Dr. Feraru's impression was probable C7 radiculopathy, diplopia due to eyestrain, history of pituitary adenoma, and degenerative disc disease. *Id.* at 23. She ordered an MRI of petitioner's cervical spine and a follow up appointment. *Id.*

A cervical spine MRI performed on September 19, 2007 showed a 1.0 cm enhancing lesion at the C3 level on the left. Pet. Ex. 5 at 3-4. The impression was the lesion could be consistent with an acute demyelinating plaque. *Id.* at 4. A slightly larger non-enhancing lesion on the thoracic spinal cord was also found, indicating a chronic demyelinating plaque. *Id.* A brain MRI was recommended to evaluate the possibility of multiple sclerosis. *Id.*

Petitioner returned to Dr. Feraru on October 10, 2007. Dr. Feraru noted that upon review of petitioner's January 2007 brain MRI, there was one small possible lesion in the lateral ventricle. Pet. Ex. 7 at 26. A visual evoked response exam indicated possible optic neuritis on the right. *Id.* Dr. Feraru's impression was that the cervical MRI was consistent with a diagnosis of multiple sclerosis, along with symptoms of paresthesia, fatigue, and perhaps blurry vision. *Id.* Petitioner was scheduled for a lumbar puncture with the hope of starting treatment for MS if the lumbar puncture results confirmed the diagnosis. *Id.*

Petitioner's cerebrospinal fluid from a lumbar puncture performed on October 15, 2007 was positive for oligoclonal bands. Pet. Ex. 7 at 28. Dr. Feraru started petitioner on Rebif and Provigil on November 6, 2007 to treat her MS. *Id.*

On January 7, 2008 petitioner visited the Multiple Sclerosis Specialty Clinic at Wake Forrest University for a second opinion regarding her MS diagnosis. She reported difficulty with her vision over the previous months, as well as fatigue, neck pain, and other similar symptoms. Pet. Ex. 21 at 2. Dr. Douglas Jeffrey, who examined petitioner, confirmed that there were lesions on her brain and cervical MRIs, consistent with MS. *Id.* Dr. Jeffrey agreed with treating petitioner with Rebif. *Id.* at 4.

On January 24, 2008, petitioner underwent a brain MRI requested by Dr. Feraru. The MRI revealed two lesions in the periventricular white matter. Pet. Ex. 5 at 1. One of the lesions was present on a previous scan; however the other was a new presentation. *Id.* Neither of the lesions was enhancing. *Id.* Petitioner reported to Dr. Feraru on an office visit four days later that she had a recent episode of left leg and left arm tingling for about twenty-four hours, and that it later resolved. Pet. Ex. 7 at 29. Dr. Feraru's impression was that her MS was "fairly stable," with some improvement of her neck pain and headaches. *Id.* at 30.

Dr. Feraru again noted petitioner's MS was stable on June 9, 2008. Pet. Ex. 7 at 26. Petitioner continued treatment through December 2008 for thyroid and pituitary symptoms, fatigue, neck pain, and headaches. In February 2009, petitioner underwent a brain MRI which revealed a new lesion in her left frontal subcortical white matter. Pet. Ex. 11 at 1. The radiologist noted a "regression of the previously noted enhancing white matter lesion . . . with only a small area of gliosis remaining." *Id.* A thoracic MRI showed a lesion at T2-3, which was consistent with a chronic MS. *Id.* at 4. Additionally, a cervical MRI revealed evidence of chronic MS. *Id.* at 6. Repeat MRIs in August 2009 revealed a new enhancing lesion about 6-7 mm in size on her cervical MRI, as well as a slightly larger demyelination as compared to her February 2009 MRI. Pet. Ex. 33 at 41. A lumbar MRI revealed disc herniation and annular tearing. *Id.* at 16.

Petitioner began treating her MS with Copaxone in February 2010. Pet. Ex. 27 at 16. She was treated with IV Solu-Medrol at Randolph Hospital from April 11 to 13, 2011 and from August 24 to 26, 2011. Pet. Ex. 33 at 29-34, 39-41. Petitioner continued care with her primary care physician, Dr. Haque, and neurologist, Dr. Denis Hill through 2012.

Dr. Haque provided a letter in 2011 that set forth his opinion that it was more likely than not that the Hepatitis B vaccine caused or substantially contributed to her condition. *See* Pet. Ex. 30 at 1. He noted that Ms. Smith had been his patient since October 2004 and he had witnessed a dramatic change in her over this time from a hardworking and compliant patient to one suffering from many complications of MS. *Id.* He noted that initially she exhibited multiple vague neurological symptoms shortly after the vaccination series which were at first less frequent and small, but progressed over time. *Id.*

II. EXPERT OPINION AND CAUSATION ANALYSIS

A. Issue to be determined

The issue to be determined is whether a Hepatitis B vaccination petitioner received on December 20, 2005 caused her multiple sclerosis. Petitioner offers the testimony and expert reports of Dr. Lawrence Steinman on her behalf. Respondent disputes that the vaccination played any role in causing petitioner's condition and further argues that petitioner had symptoms of multiple sclerosis before her December 2005 vaccination. Respondent offers the testimony and expert reports of Dr. David Alexander.

B. Legal Standard

The Vaccine Act established the Program to compensate vaccine-related injuries and deaths. § 300aa-10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" *Rooks v. Sec'y of HHS*, 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

In order to prevail under the Program, a petitioner must prove either a "Table" injury or that a vaccine listed on the Table was the cause infact of an injury (an "off-Table" injury). An "off-Table" injury is initially established when the petitioner demonstrates, by a preponderance of the evidence that: (1) she received a vaccine set forth on the Vaccine Injury Table; (2) she received the vaccine in the United States; (3) she sustained or had significantly aggravated an illness, disease, disability, or condition caused by the vaccine; and (4) the condition has persisted for more than six months. § 13(a)(1)(A). There is no dispute that petitioner received a covered vaccine in the United States and that she has suffered from multiple sclerosis for more than six months.

To satisfy her burden of proving causation in fact, petitioner must establish each of the three *Althen* factors by preponderant evidence: (1) a medical theory causally connecting the vaccination and her injuries; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injuries; and (3) a proximate temporal relationship between the vaccination and the injuries. *Althen v. Sec'y of HHS*, 418 F.1274, 1278 (Fed. Cir. 2005); *see de Bazan v. Sec'y of HHS*, 539 F.3d 1347, 1351-52 (Fed. Cir. 2008); *Caves v. Sec'y of HHS*, 100 Fed. Cl. 119, 132 (2011), *aff'd per curiam*, 463 Fed. Appx. 932 (Fed. Cir. 2012) (specifying that each *Althen* factor must be established by preponderant evidence). The preponderance of the evidence standard, in turn, has been interpreted to mean that a fact is more likely than not. *See Moberly v. Sec'y of HHS*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. *Bunting v. Sec'y of HHS*, 931 F.2d 867, 873 (Fed. Cir. 1991). "[T]he purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body." *Althen*, 418 F.3d at 1280.

Once petitioner establishes each of the *Althen* factors by preponderant evidence, the burden of persuasion shifts to respondent, who must show that the alleged injury was caused by a factor unrelated to the vaccination. *Knudsen v. Sec'y of HHS*, 35 F.3d 543, 548 (Fed. Cir. 1994); § 13(a)(1)(B). Respondent must demonstrate that "the factor unrelated to the vaccination is the more likely or principal cause of the injury alleged. Such a showing establishes that the factor unrelated, not the vaccination, was 'principally responsible' for the injury." *Deribeaux v. Sec'y of HHS*, 717 F.3d 1363, 1369 (Fed. Cir. 2013). Section 13(a)(2) specifies that factors unrelated do "not include any idiopathic, unexplained, unknown, hypothetical, or undocumented causal factor, injury, illness, or condition." Close calls regarding causation must be resolved in favor of the petitioner. *Althen*, 418 F.3d at 1280.

In determining whether petitioner is entitled to compensation, a special master must consider the entire record and is not bound by any particular piece of evidence. § 13(b)(1) (stating a special master is not bound by any "diagnosis, conclusion, judgment, test result, report, or summary" contained in the record). Thus, a special master must weigh and evaluate opposing expert opinions, medical and scientific evidence, and the evidentiary record in deciding whether petitioners have met their burden of proof.

> Although *Althen* and *Capizzano* make clear that a claimant need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act, where such evidence is submitted, the special master can consider it in reaching an informed judgment as to whether a particular vaccination likely

> caused a particular injury . . . . Medical literature and epidemiological evidence must be viewed, however, not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard."

Andreu v. Sec'y of HHS, 569 F.3d 1367, 1380 (Fed. Cir. 2009) (internal citation not included).

C. Expert Qualifications

1. Petitioner's Expert, Lawrence Steinman, M.D.

Dr. Lawrence Steinman is a board-certified neurologist. Pet. Ex. 44 at 2. He received an undergraduate education at Dartmouth College and obtained his medical degree from Harvard Medical School. Tr. at 67. After medical school, he completed an internship in surgery and residency in pediatric and adult neurology at Stanford University. *Id.*; Pet. Ex. 44 at 1. In 1980, Dr. Steinman joined the faculty at Stanford University Medical School and is currently the George A. Zimmerman Professor of Genetics, Pediatrics, Neurology and Neurological Sciences. Tr. at 67. His research is focused on Multiple Sclerosis and related diseases. *Id.* He holds over twenty-three patents related to his research, and has authored a significant number of medical articles. *See generally* Pet. Ex. 44. He is an invited member in the Institute of Medicine section of neurology. Petitioner offered and I accepted Dr. Steinman as an expert in neurology, particularly Multiple Sclerosis. *Id.* at 83. Respondent did not object. *Id.*

2. Respondent's Expert, David Alexander, M.D.

Dr. David Alexander is a board-certified neurologist, with a subspecialty in vascular neurology and spinal cord medicine. Respondent's Exhibit ("Res. Ex.") B at 2; Tr. at 184. He received an undergraduate degree from Amherst College and a medical degree from the University of Minnesota Medical School. Res. Ex. B at 1. Thereafter, he completed an internship in medicine at Boston University Medical Center and residency in neurology at Columbia Presbyterian Medical Center in New York. *Id.* He is currently a clinical professor of neurology at the University of California Los Angeles ("UCLA") David Geffen School of Medicine. *Id.* at 2; Tr. at 181. He is also the Director of the Neurological Rehabilitation and Research Unit at UCLA Medical Center, and Associate Director of the neurology residency training program at UCLA. Res. Ex. B at 2; Tr. at 181. Dr. Alexander has conducted research projects in various areas, including stroke rehabilitation, and has authored chapters in medical textbooks and journal articles related to his subspecialty interest in rehabilitation. Tr. at 182-83. In his clinical practice, Dr. Alexander routinely treats patients with neurological diseases, including patients with multiple sclerosis. Tr. at 184-85. Respondent offered and I accepted Dr. Alexander as an expert in neurology. *Id.* at 186. Petitioner did not object. *Id.*

D. Causation Analysis[4]

1. Onset of MS Symptoms

In this case, the parties presented two highly qualified experts. The petitioner presented Dr. Steinman, one of the most well regarded experts in multiple sclerosis in the world, who has focused on research into understanding the disease and developing treatments for it, and who also has seen and treated many multiple sclerosis patients over his career. Dr. Alexander is a clinical neurologist and Professor of Neurology, who has also seen and treated many multiple sclerosis patients. The testimony to a large extent debated the date of onset of Ms. Smith's condition, and illustrated the frustration involved in determining the time of onset of MS. Both doctors agree unequivocally that Ms. Smith has diagnosable multiple sclerosis at this point. In fact, the evidence of progression from a single enhancing lesion seen on MRI in May 2006, to an enhancing C3 lesion and an older thoracic lesion in October 2007, to multiple lesions in the spine and brain in 2009, to many lesions by 2011, shows significant progression of the disease. Dr. Steinman presented the theory of molecular mimicry (with supporting literature) between the Hepatitis B vaccine and damage to myelin; and in particular, to a component of myelin known as myelin oligodendrocyte protein ("MOG"), which is critical to the manufacture of myelin. Dr. Steinman opined that the onset of petitioner's multiple sclerosis occurred between four days and approximately forty-two days after the vaccination which he considered appropriate for MS to be caused by the vaccine. Tr. at 109. There was no testimony offered in disagreement about the appropriateness of this timing, if it was assumed that the disease onset occurred consistent with Dr. Steinman's opinion.

The heart of the dispute focused on when Ms. Smith's disease began. Based on his review of the records, Dr. Steinman believed that the onset began between Christmas Eve of 2005 and the end of January or early February of 2006. Dr. Alexander contended, based on his review of the records, that Ms. Smith was actually suffering from MS as early as 2003, if not before. Ms. Smith received the third Hepatitis B vaccination on December 20, 2005.

The National Multiple Sclerosis Society, on its website, discusses the difficulty with diagnosing MS in its early stages as the symptoms can be quite non-specific, or in other words, possibly explained by MS but also possibly explained by the clinical presentation of any number of other conditions, injuries or diseases.[5] The same website lists common symptoms of MS, including fatigue, numbness and tingling, dizziness or vertigo, visual disturbances, gait, bladder and sexual problems, pain, weakness, spasticity, emotional changes, clinical depression and

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[4] I have considered the entire record in arriving at my decision (§ 300aa–13(a)(1)). This includes extensive medical literature submitted by both parties which I have read and considered. I will discuss in the course of this opinion the exhibits that are most relevant to the resolution of this case.

[5] *See* NATIONAL MULTIPLE SCLEROSIS SOCIETY, *MS Symptoms*, www.nationalmssociety.org/symptoms-diagnosis/MS-symptoms/ (last visited Apr. 18, 2016).

cognitive deficits. *Id.* The key diagnostic criteria for MS, as set forth in the McDonald criteria of 2010 (which was referenced by both doctors even though neither side marked the document as an exhibit) is that symptoms lasting at least twenty-four hours must occur at different locations in the body and at different times, and not be explained by other diagnosable conditions.[6] Though Dr. Alexander strongly argued that the diagnosis can be made clinically without the benefit of MRI imaging, he acknowledged that very few such diagnoses are made without MRI. Tr. at 258. The McDonald panel of experts indicated that most often the diagnosis is confirmed by MRI imaging of lesions in the brain or spine that occur at different times. *See supra* note 6. The timing of the lesions can be determined by the appearance of new lesions on serial scans or by the presence of gadolinium enhancing lesions and non-enhancing lesions on a single scan. *Id.* Dr. Alexander testified that demyelinating lesions will enhance for up to four to six weeks after their initial occurrence; after that, they either will not enhance, may turn to plaque, or even completely disappear. Tr. at 210-11.

Additionally, MS may present in a remitting–relapsing form or a progressive form. The remitting–relapsing form of the disease, coupled with the non-specificity of the presenting symptoms, creates significant diagnostic difficulty particularly for non-neurologists or even for many neurologists who do not have particular experience with MS. Upon review of all of the testimony, it is apparent there would be no disagreement between Dr. Steinman and Dr. Alexander on these general statements about MS. The problem arises in their respective interpretations of Ms. Smith's medical history.

There is no dispute that none of the treating doctors diagnosed multiple sclerosis before an enhancing 0.8 cm lesion in the temporal lobe of Ms. Smith's brain was seen on a May 2006 MRI. Tr. at 233. In fact, a definitive diagnosis as consistent with MS was not made until Dr. Elaine Feraru, a treating neurologist, did so on October 10, 2007. Pet. Ex. 7 at 26. At that time Dr. Feraru noted that Ms. Smith was a thirty-five-year-old woman complaining of paresthesias, numbness, tingling down arms, and fatigue. *Id.* at 25. She also wrote that occasionally Ms. Smith got diplopia (double vision) and sometimes got ptosis (drooping eyelid) of the right eye when tired. *Id.* She got some headaches and her pupils were equal and "slightly reactive." *Id.* Dr. Feraru reviewed brain and spine MRIs, which had just been completed, and noted a slightly enhancing lesion behind the C3 vertebral body and another enhancing lesion at T2. *Id.* at 26. She noted that on an MRI from January of that year there appeared one very small periventricular, possible lesion, on the right, adjacent to the anterior horn of the right lateral ventricle. *Id.* She noted that the MRIs were consistent with the diagnosis of MS. *Id.* By February 18, 2011, an MRI of the brain showed multiple lesions with many oriented perpendicularly to the corpus callosum with a rim enhancing lesion on the corona radiata and an

[6] *See* NATIONAL MULTIPLE SCLEROSIS SOCIETY, *Tip Sheet 2010 Revised McDonald Diagnostic Criteria for MS: Diagnosis of MS Requires Elimination of More Likely Diagnoses and Demonstration of Dissemination of Lesions in Space and Time, available at* http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Paper-TipSheet_-2010-Revisions-to-the-McDonald-Criteria-for-the-Diagnosis-of-MS.pdf (last visited Apr. 18, 2016).

enhancing lesion in the left frontal lobe. Pet. Ex. 28 at 1-2. At that point, the presentation was entirely typical of multiple sclerosis. *Id.*

In his testimony, Dr. Steinman accepted the testimony of Ms. Smith's college age daughter, Kaitlyn Tedder, that her mother became quite symptomatic at Christmas of 2005 and that she began to endorse visual symptoms in that time period and thereafter. Tr. at 132. He also accepted the medical record from May 1, 2006 in which the history indicated that she had suffered from dizziness, visual impairment and fatigue for about three months. Pet. Ex. 3 at 50. Consistent with Dr. Steinman's opinion, Ms. Smith testified that she had experienced back pain initially after a car accident in 1994, when hit by a drunk driver, and again after a car accident in 2003. Tr. at 32. Both times she was pregnant. *Id.* She also had significant lumbar back pain in December of 2003 when she was nine months pregnant and saw Dr. Ford. *Id.* She also attributed upper back pain in the past to scoliosis. *Id.* Records do indicate that she had physical therapy for upper back pain prior to the December visit with Dr. Ford, when Dr. Ford mentioned that he had seen her in September for thoracic pain. *See* Pet. Ex. 4 at 62.

Ms. Smith described a significant increase in her pain symptoms in her neck when she went back to work in January after the Christmas incident. Tr. at 33. At that time she thought the neck pain was attributable to handling eighty-five to ninety calls a day at work without having the benefit of a headset, as she had had when she worked a similar job at American Express. *Id.*

Ms. Smith also appeared to have suffered some significant cognitive deficits, as she had gone from being a person who could perform a clerical job in a hospital to someone who, despite the valiant efforts of counsel to focus her, had difficulty presenting a coherent history from the witness stand. It should be noted that prior to the entitlement hearing held before me, a fact hearing in which Ms. Smith alone testified was held before Special Master Hastings in November 2011. After a review of that transcript, I strongly encouraged counsel during a status conference to work with Ms. Smith to present clear testimony at this hearing, as the prior transcript was virtually impossible to understand. At the entitlement hearing, it was clear to me that counsel had endeavored to help Ms. Smith to testify more clearly, but as observed by both experts, the most that could be derived from the testimony were some scattered factoids and an opaque history. Tr. at 205-06; 284-85. Dr. Steinman acknowledged that the difficulty in obtaining a crisp history can be one of the challenges in MS diagnosis, and Dr. Alexander noted that frequently minor symptoms of MS are missed by treating physicians. *Id.* at 81, 201-02.

To remedy that problem, petitioner presented the testimony of Kaitlyn Tedder. Kaitlyn, Ms. Smith's daughter, is a college student at Wingate University in North Carolina in a program from which she will receive a doctor of pharmacy degree upon completion. Tr. at 51. She testified that at Thanksgiving of 2005 she, her little brother, and her mother observed all of their normal family traditions. *Id.* at 53-54. Her mother drove them for 30 minutes to Denton, North Carolina from Asheboro where they lived. *Id.* at 53. Her great grandmother lived in Denton where they had their first Thanksgiving dinner around midday. *Id.* They then drove back to Asheboro and had a second dinner at their grandmother's house which was their normal tradition. *Id.* Kaitlyn said everything was normal that day. *Id.* at 53-54. However, on Christmas a month later, things were much different. Kaitlyn, who was eleven at the time, woke

up early with her two-year-old brother to open presents. *Id.* at 55. They went in to get their mother and she said she was not feeling too well, and asked if they would wait another hour. *Id.* As the day went on Ms. Smith could not get up and they waited a few hours. *Id.* at 56. Finally, her mother said to go ahead downstairs without her. *Id.* They went downstairs and their presents were not wrapped which had never occurred before. *Id.* Kaitlyn testified that it was also the family tradition to go to their grandmother's house at lunch time on Christmas day where they would have their meal and play with all their cousins. *Id.* On this day, however, they were unable to get their mother going until the later afternoon and by the time they arrived at their grandmother's, everyone but one aunt had already gone home. *Id.* at 56-57.

At the fact hearing in November 2011, Ms. Smith said that she had experienced some visual spots in the shower after the second Hepatitis B shot in July, which resolved; but at Christmas, when she tried to wash her hair in the shower, she saw more spots and her neck started hurting a lot. *See* Fact Transcript ("Fact Tr.") at 23. She then added at the entitlement hearing, that around Christmas when she took a shower, she had visual disturbances, and dizziness, and had to lie down before she could get dressed. Tr. at 15. Ms. Smith testified that while driving home after dark that night, she experienced a frightening episode of double vision in which she saw two cars coming at her simultaneously. *Id.* at 17-18. She had never experienced this before. *Id.* at 17. The medical records note that sometime after that she began to experience impaired vision which she described as blurry vision. *See* Pet. Ex. 3 at 50. Both she and Kaitlyn testified that she began to have difficulty reading things and that she was constantly buying over the counter glasses after that time which she had never worn before. Tr. at 38-40, 54-55, 58-59.

Dr. Steinman acknowledged the difficulty of establishing the clinical onset of multiple sclerosis. Tr. at 141. He said that it is usually dated from the occurrence of some acute event, but it may have been building for some time. *Id.* at 141-42. He described the process of establishing a timeline as identifying a series of "handholds" in the history. *Id.* at 123. He definitely thought that the Christmas episode as described by Kaitlyn represented a handhold. *Id.* Dr. Alexander disagreed. *Id.* at 205-07, 235. I find that Kaitlyn testified very credibly and cogently. I find it very difficult to believe that a woman who from all appearances was otherwise a loving and competent mother of an eleven year old and a two year old would not wrap their Christmas presents, would not come down with them on Christmas morning, and could not get herself started to the grandmother's house until hours after their due time, did not have some significant health issue going on as she described. Her description of the driving incident was also rather clear, and she described it as double vision, although Dr. Alexander doubted that it actually was. *Id.* at 236. He thought this was a refractive error coming on at night that made headlights look large. *Id.* Dr. Steinman acknowledged that it was difficult to completely understand what was happening with her vision from her testimony, but noted that it would be unusual for a refractive error, such as an astigmatism, to come on suddenly. *Id.* 279-80. He thought that the double vision could have been caused by abnormalities in the pathways that control conjugate vision in the pons in the medial longitudinal fasciculus and that it could have been a lesion that passed within a few weeks. *Id.* at 283. He said this could be caused by MS. *Id.* 125.

Dr. Alexander doubted the significance of the Christmas incident as a "handhold" for MS. Tr. at 205-07. He believed that she had a relapsing–remitting form of MS, which began long before December 20, 2005. He noted that she complained of mid-back pain to her obstetrician in August 2004. *Id.* at 194. In his view, one of the most important pieces of evidence was Dr. Ford's neurology note in December 2003, when Ms. Smith was thirty-eight weeks pregnant and was hospitalized overnight with severe lumbar sacral back pain. *See* Pet. Ex. 4 at 62. Dr. Ford noted that Ms. Smith had suffered from back pain since 1994. *Id.* She had apparently been managed by another doctor in his office prior to September of 2003 when Dr. Ford initially saw her. *Id.* Dr. Ford noted that her pain had been primarily in the interscapular area but was not on this day in December when she was suffering severe low back pain with pain radiating down her left leg to the knee but not below. Pet. Ex. 4 at 62. Dr. Ford reviewed the note of a prior MRI of the lumbar spine from February 2002 which showed mild disc desiccation at L4-L5 and L5-S1 with a mild bulge of the L5-S1 disc, and a small central annular tear at L4-L5. *Id.*; s*ee* Pet. Ex. 4 at 83. The reading radiologist at the time of the February 2002 MRI noted that this tear could be the source of focal pain. Pet. Ex. 4 at 83. As Ms. Smith's pain was improving when Dr. Ford saw her a day after admission, on December 4, 2003, and she did not want an epidural while she was nine months pregnant, he discharged her on Vicodin. Pet. Ex. 4 at 62. Both Dr. Steinman and Dr. Alexander agreed that it is common in relapsing–remitting MS to have a remission in MS symptoms in the last trimester of pregnancy. Tr. at 303-04, 307.

Dr. Alexander placed enormous weight on a patient history form that was filled out at a December 2003 evaluation in which the words "spots 7/03" were written beside the category vision. Tr. at 191; *see* Pet. Ex. 4 at 71. Dr. Alexander argued that these words must have been written by Ms. Smith and that the fact that she wrote them on a form five months later suggested that these were very significant and were not just spots seen on standing up. Tr. at 191-92. He thought that the mention of spots in July 2003 suggested that Ms. Smith might have meant they lasted all month even though he acknowledged that the record said no such thing and the neurologist did not make any further record of evaluating that symptom. *Id.* at 241. At the same time he discounted the entry on the May 2006 chart which stated dizziness, vision impairment and fatigue over three months as possibly having been written by an MRI tech. *Id.* at 237. There was no other mention of the spots symptom anywhere in the medical record. Dr. Alexander believed that these spots could have been a scotomata which could be an MS symptom. *Id.* at 191-92. Dr. Steinman did not disagree that they could be but stated that spots are very non-specific and can occur with various forms of headache, with getting up quickly, or could be floaters. *Id.* at 268-70.

Ms. Smith testified that after Christmas 2005, she began having chronic visual issues. Tr. at 34-42. She described them as blurry vision. *Id.* at 36. She testified that she began buying over-the-counter glasses to help with this problem. *Id.* at 38. She was hoping to get a tinted screen on her computer at work as she was noting visual problems there which she attributed to the computer screen. *Id.* at 16. She also experienced significant neck pain in the early months of 2006 which she thought might have been occurring because she was answering eighty-five to ninety calls a day at work and had not been provided with a headset. *Id.* at 33. Kaitlyn testified that her mother began having vision problems during this time and would ask her to read things for her. *Id.* at 58-59. She also said she was always complaining about neck pain which she had not before. *Id.* at 61. Ms. Smith described incidents in January 2006 of visual spots upon going

into light and when she was in the shower. *Id.* at 34-35. She said when she got heated it was like having flies all around her. *Id.* 35. These symptoms are common in MS.

Ms. Smith delivered a baby on December 10, 2003, five days after seeing Dr. Ford. *See* Pet. Ex. 4 at 18. In further support of his opinion of pre-existing MS, Dr. Alexander testified that he thought the next significant event, at least to the extent documented in the medical records, appears to have happened on February 24, 2004. Tr. at 197. Dr. Alexander noted that she complained to Dr. Hassan at Randolph Hospital of numbness in the right foot and sometimes in the arms when she held the baby which, with the benefit of hindsight, he thought was likely a symptom of inflammation in the spinal cord. *Id.* Dr. Hassan did not suspect MS and diagnosed thoracic back pain, date of onset with motor vehicle accident on June 17, 2003. *See* Pet. Ex. 3 at 10. He noted her history of scoliosis and bulging discs. *Id.* She also complained of occasional pain in the left leg. *Id.* Interestingly, Dr. Ford had ordered MRIs to the cervical, lumbar and thoracic spine that were performed on February 19, 2004. The films, done without contrast, did not identify any MS lesions or plaques on any of the studies. *See* Pet. Ex. 5 at 7-10. The MRI films showed small disc protrusions at C5-6 and C6-7. *Id.* at 9. The thoracic films noted minimal disc bulges midline more to the right at T5-6 and T6-7 which did not impinge on nerve roots or the central canal. *Id.* at 9. The report of the lumbar spine MRI indicated the presence of a small disc bulge at L4-5 and another at L5-S1 with a small central annular tear at that level. *Id.* at 8.

A physical therapy record from February 24, 2004 contained a sketch of the posterior human figure showing back pain from shoulders to the upper pelvic area. Pet. Ex. 3 at 18. During the month of March that year a similar sketch on the physical therapy chart showed pain in the shoulders but not below as before. *Id.* at 19. On April 7, 2004, Dr. Ford prescribed physical therapy three times a week for two weeks. *Id.* at 8.

In another significant record in Dr. Alexander's reconstruction of what he believed was Ms. Smith's history of relapsing–remitting MS was an emergency room note from June 1, 2004 for low back pain. In the history section of the note she reported no numbness or tingling. Pet. Ex. 3 at 25. The physical examination section of the note stated: "There is decreased Achilles on the left. *She reports* decreased sensation in her entire left leg. Heel-toe intact. There is positive [sic] for equivocal straight leg raising on the left." *Id.* (emphasis added). It was also noted that "She has pain at the lumbo-sacral junction." *Id.* The note was signed by Kim Lykins, D.O., the same physician who saw Ms. Smith in the emergency room the year before when she presented after a motor vehicle accident with symptoms of back pain. Dr. Alexander found the loss of sensation in the entire left leg to be a significant handhold for MS. Tr. at 199-200. He believed that despite the fact that the note reported findings such as decreased Achilles and equivocal straight leg raising (which would be more consistent with disc or peripheral nerve pathology) and the reference to decreased sensation in the leg was preceded by the words "she reports," that this was also a finding indicating that she told the doctor that she had decreased sensation after he tested for it. *Id.* Dr. Alexander testified that he thought this finding was a very significant suggestion of an MS lesion in the thoracic spine which he did not think could be explained by degenerative disc disease. *Id.* at 200-01. He said that when someone endorses decreased sensation in the entire left leg, it sounds like it is coming from inflammation in the spinal cord and not from a disc or discs. *Id.* He noted that back pain in the interscapular area is

an unusual place for back pain and that back pain in this location was most likely explained by inflammation or an MS lesion in the thoracic spine. *Id.* at 194-96.

Dr. Steinman "vehemently disagreed" with Dr. Alexander's interpretation of this note. Tr. at 273. He said that if leg sensory issues were as interpreted by Dr. Alexander, any neurologist would have taken his exam with the pin over the leg into the lower abdomen and thorax. *Id.* at 273-74. Loss of sensation in the entire left leg caused by a thoracic lesion would also give rise to loss of sensation in these areas. *Id.* None was reported. *Id.* He said that if there was inflammation in the thoracic spine he would expect hyperactive reflexes and upgoing toes but none of this was reported. *Id.* at 274-75. In Dr. Steinman's opinion, this note could be explained by "pure and simple L5-S1 degenerative disc disease." *Id.* at 275. It should be noted that a positive straight leg raising test is suggestive of lumbar disc pathology. Asked by the undersigned how he would explain the interscapular back pain, Dr. Steinman replied that back pain is a very common phenomenon and that he highly doubted the whole leg loss of sensation claim. *Id.* at 299-300. He thought that the degenerative disc disease, which albeit mild, was demonstrated on the MRI at multiple levels. *Id.* at 272-73. Dr. Alexander agreed that lumbar and cervical back pain is common, but not so much interscapular pain. *Id.* at 259-60. Dr. Alexander believed that the interscapular pain and the whole leg loss of sensation were caused by a thoracic lesion that was seen on MRI more than three years later in October 2007, but did not note that no such lesion was seen on the February 2004 MRI. Interscapular back pain is less common than cervical or lumbar pain but not completely unusual, and it should be noted that the MRI had identified degenerative thoracic discs which are also less common than bulging discs in the cervical or lumbar areas.

Dr. Alexander ultimately opined that MS was clinically diagnosable in 2004 with the combination of interscapular back pain, the loss of sensation in the left leg, and the mention of spots in July. Except for the back pain, which appeared to occur as often in the lumbar spine as anywhere else, the clinical symptoms, prior to the vaccination, were mentioned on one occasion only, and in the case of the visual symptom, only in a history form filled out five months after the reported event. Neither the mention of spots nor the "reported decrease in sensation" in the left leg prompted any further investigation by the treating physicians. No notations were made by the physicians to document whether the spots in July or the deceased sensation in the left leg had lasted for more than 24 hours.

Dr. Steinman attached greater significance to the events described by the petitioner and her daughter at Christmas 2005, five days after Ms. Smith received the third Hepatitis B vaccine. Dr. Steinman saw this event as the beginning of a change in trajectory. Tr. at 122-24. While he could not completely discount the possibility that the earlier symptoms identified by Dr. Alexander were possible MS symptoms, he opined that they were very non-specific, could just as readily be explained by other common explanations such as degenerative disc disease, a motor vehicle accident, low back pain secondary to the ninth months of pregnancy and so forth. None of the treating physicians raised any question of MS when these events occurred including the neurologist, Dr. Ford. Tr. 281. The next question then became: what evidence of the change in trajectory could he identify in the months immediately following the vaccination? Other than the mention of spots on the vision line in 2003, both doctors agreed that there was no mention of visual symptoms prior to Christmas of 2005. *Id.* at 239-40. Dr. Alexander doubted Ms. Smith's

description of double vision while driving home on Christmas night. *Id.* at 236. He thought this was more likely the result of refractive error or basically visual decline that is common with age. *Id.* Ms. Smith, however, testified that this was a very frightening incident in which she perceived that a car was coming directly at her when she had both of her children in the car. *Id.* at 17-18. Kaitlyn testified that she did not recall her mother complaining of visual problems before that Christmas and did remember that this complaint became common afterward. *Id.* at 58-59. She said that she recalled her mother complaining of double vision, not being able to see and grabbing her neck a lot between Christmas 2005 and May 2006. *Id.* at 59-61. She said her mother never wore glasses before that time and afterwards frequently bought non-prescription glasses to aid with vision. *Id.*

Dr. Alexander contended that the description given by Kaitlyn of her mother using glasses to help with vision supported the argument that her visual issues were the result of normal aging and were refractive errors. Tr. at 203-04. Ms. Smith did not have an eye examination until October 2006, when she reported at Academy Eye Center that she had been experiencing double vision, blurry vision and night blindness. Pet. Ex 16 at 1, 3. Her unaided eye exam was 20/30 in both eyes, not a very significant refractive deficit. *Id.* at 2. She was diagnosed with hyperopia and astigmatism. *Id.* at 1; Tr. at 139.

Dr. Steinman testified that the description of the visual issues was frustrating. Tr. at 128-29. Ms. Smith did have a borderline evoked potential in one eye shortly after the May 2006 MRI. *Id.* at 137-40. The visual evoked potentials result would be consistent with MS. He agreed that the use of glasses likely suggested refractive error but testified that that did not exclude MS caused visual symptoms. *Id.* at 128, 139-40. While the symptoms as described were not classical MS visual symptoms, they were also not inconsistent with MS, and the refractive deficit could have been co-existent with the MS-caused symptoms in early 2006.

Between Christmas 2005 and the May 2006 MRI which demonstrated a 0.8 cm enhancing lesion in the temporal lobe of Ms. Smith's brain (which Dr. Steinman and Dr. Alexander agree was an MS lesion and the first one to be identified in the petitioner) the symptoms recorded in the medical records were not terribly suggestive of a diagnosis. Ms. Smith saw her family physician, Dr. Haque. She reported fatigue which would be consistent with MS but also of many other things. Dr. Haque initially treated her for a virus or the flu. Pet. Ex. 31 at ¶ 7. In May 2006, she sought treatment at Randolph Hospital suggesting that the symptoms had become much more severe and not what had been called the flu before. *Id.* The note at the hospital says dizziness, vision impairment and fatigue over three months, which Dr. Alexander did not dispute but he discounted the record as possibly having been written by an MRI technician. Tr. at 237. It should be noted that he had no basis in the record to draw that conclusion and regardless of who wrote the note, the history must have come from Ms. Smith. He did doubt that the dizziness symptom, which could be caused by MS, would be explained by a temporal lobe lesion. *Id.* at 208. Dr. Steinman testified that in retrospect the diagnosis of MS was confirmed in 2007 but that the first radiologic evidence of it was the May 2006 MRI. *Id.* at 131-32. He testified that even with a "retrospectoscope" MS was not diagnosable in 2003 as suggested by Dr. Alexander. *Id.* at 262-63, 280-81. There was nothing that provided objective evidence of a lesion in the thoracic spine and he thought that she had classic L5-S1 neuropathic pain referable to objective data on the MRIs done in 2004, which demonstrated mild bulging

discs in the cervical, thoracic and lumbar spine (and no MS lesions). *Id.* at 281-82. He thought that Ms. Smith's testimony about seeing two cars coming at her while driving home on Christmas night could suggest abnormalities in the pathway that controls conjugate vision. *Id.* at 283. He said that diplopia can be a symptom of MS and that some visual acuity issues can also be caused by MS. *Id.* at 283-84. He noted that even if an astigmatism would explain some of her visual issues, an astigmatism does not happen suddenly as the onset of visual symptoms did in this case. *Id.* at 279-80. Other than the visual symptoms, dizziness, and fatigue, he did not see new symptoms of MS between Christmas 2005 and May 2006 but thought that the three-month history of dizziness, visual problems and fatigue given in May was consistent with a post-vaccine onset of MS. *Id.* at 108-09. Further the lesion identified on MRI was objectively new as it was enhancing on May 1, 2006. Both doctors agreed that a lesion would not enhance if it were older than four to six weeks. *Id.* 105-06, 209-10.

Dr. Steinman placed considerable weight on the diagnoses reached by Drs. Ford, Dr. Haque and other treating physicians. Both experts agreed that MS can be difficult to diagnose and can be missed because of the vague nature of the symptoms. To be sure, defining the date of onset of Ms. Smith's disease was not only handicapped by her inability to present cogent and coherent testimony, but also suffered from the lack of detailed medical histories that included follow-up on the mention of issues like double vision, blurry vision, dizziness and back pain. It does not appear that any of the treating physicians suspected MS prior to May 2006, when the initial lesion was identified. While Dr. Alexander suggested that Dr. Ford may have noted the fact of prior interscapular back pain in December 2003, when Ms. Smith was in the hospital for lumbar pain, as possibly suggesting that he was thinking about such a possibility, there is no evidence that that was the case and if anything the evidence is to the contrary in that he ordered MRIs of the entire spine in February 2004 but did not order gadolinium contrast which almost certainly would have been ordered if MS was on his differential diagnosis at the time.

Dr. Steinman testified that he believed that Ms. Smith suffered from a relapsing-remitting form of MS which became a secondarily progressive form of the disease as evidenced by the increase in symptoms through 2006 and the dramatic increase in identified lesions by October 2007 with oligoclonal bands on spinal tap. Ms. Smith's affidavit and testimony, along with the more precise testimony of her daughter, suggested new and worsening symptoms consistent, at least retrospectively, with MS during the first five months of 2006. This testimony was supported by the medical record indicating three months of consistent symptoms that had been become sufficiently troublesome by May 1, 2006 that she went for treatment, and that were sufficiently concerning at that time to have caused the physician to order a brain scan.

While it is almost impossible to definitively decide that the diagnostic approach of either Dr. Steinman or Dr. Alexander is right or wrong, and both doctors make plausible arguments for their opinions, the Federal Circuit has said that close calls in this program should be decided in favor of the petitioner. *Althen*, 418 F.3d at 1280. I have concluded that the issue of onset in this case is a close call and virtually impossible to determine with medical certainty. But the history of increasing symptoms beginning in the end of December 2005, the lack of evidence of lesions on multiple MRIs prior to that time, and the presence of degenerative disc disease on all of her scans before that date, as well as reasonable alternative explanations for prior back pain including two motor vehicle accidents, degenerative disc disease at multiple levels, scoliosis and

advanced pregnancy, is sufficiently persuasive to conclude that her MS began in late December 2005 with symptoms occurring, and objective lesions appearing, in the months and years afterward.

2. *Althen* Prong One

Dr. Steinman is recognized as a major authority in the field of multiple sclerosis. He has devoted a substantial amount of his career to research and treatment of the disease. He has proposed in this case and others the theory of molecular mimicry to explain the mechanism of onset of the demyelinating process in the central nervous system that becomes MS. While he candidly acknowledges that science has not yet come to the definitive answer on MS causation, he testified that molecular mimicry provides a sound and scientifically defensible explanation for the way in which some vaccines can trigger multiple sclerosis. Tr. at 74. He testified that molecular mimicry is a widely accepted theory that is taught in medical schools including Stanford University and Johns Hopkins University. *Id.* at 86. He explained that myelin is the fatty stuff that surrounds the axons in the central nervous system and insulates them like rubber on electrical wires. *Id.* 74. The insulation allows the axons to rapidly transmit information from neuron to neuron and damage to it causes disruption of that process. *Id.* He explained that myelin is composed of proteins and sugars which bear a strong chemical resemblance to the proteins and sugars in viruses and bacteria. *Id.* The theory of molecular mimicry works off this similarity between viruses and bacteria and the similar components of myelin and other body parts. *Id.* at 74-75. In his research at Stanford, Dr. Steinman has demonstrated notable similarities between myelin and viruses in position 91 of the most abundant protein in myelin, known as myelin basic protein. *Id.* He testified that Bogdanos and colleagues demonstrated another sequence between Hepatitis B and MOG,[7] which can give rise to molecular mimicry. *Id.* at 75-76; *see generally* Pet. Ex. 50.

In this case, in addition to the presentation of his own research on molecular mimicry[8] Dr. Steinman supported his theory the Bogdanos study, which demonstrated homology between the vaccine and a component of myelin which contributes to the regeneration of myelin by the oligodendrocytes in the brain. Pet. Ex. 50 at 4. Bogdanos did not find definitive connection to

[7] Bogdanos DP, Smith H, Baum H, et al., *A Study of Molecular Mimicry and Immunological Cross-Reactivity Between Hepatitis B Surface Antigen and Myelin Mimics,* 12.3 CLINICAL DEV. IMMUNOL. 217-24 (2005) [Pet. Ex. 50].

[8] *See, e.g.*, Pet. Ex. 45 (Wucherpfennig KW, Catz I, Hausmann S, Strominger JL, Steinman L, et al., *Recognition of the Immunodominant Myelin Basic Protein Peptide by Autoantibodies and HLA-DR2 Restricted T Cell Clones from Multiple Sclerosis Patients: Identity of Key Contact Residues in the B-cell and T-cell Epitopes*, 100 J. OF CLINICAL INVESTIGATION 1114-22 (1997).); Pet. Ex. 47 (Steinman L and Oldstone MBA, *More Mayhem from Molecular Mimics*, 3 NATURE MEDICINE 1321-22 (1997).); Pet. Ex. 55 (Steinman L, Axtell RC, Barbieri D, et al., *Piet Mondrian's Trees and the Evolution in Understanding Multiple Sclerosis*, *Charcot Prize Lecture 2011*, 19 MULTIPLE SCLEROSIS J. 5-14 (2013).)

MS pathology through his work, but strongly suggested that his group had made a sufficiently significant finding that more research was called for. *Id.* at 1. Dr. Steinman explained that when the immune system mis-identifies MOG as a foreign invader, which recognition is triggered by its homology with the Hepatitis B vaccine, the demyelinating process that becomes MS can be triggered in susceptible individuals. Tr. at 90-91.

Dr. Steinman testified that in the case of the Hepatitis B vaccine, the predominant cross-reactivity, as identified by Bogdanos, would be between MOG and the vaccine rather than myelin basic protein. Tr. at 91-92. He said that his own research had shown that MOG can be a significant factor in the propagation of experimental allergic encephalomyelitis and acute disseminated encephalomyelitis, which are highly related inflammatory conditions similar to multiple sclerosis. *Id.* at 91-95. The showing how an immune response to MOG will cause neuroinflammation in the human brain provides a sound scientific correlation with the development of MS. *Id.* at 92-95. He explained in response to my question, that when cross reactivity occurs in the immune response to MOG, it is affecting the oligodendrocytes which are cells that synthesize the myelin. *Id.* at 94. The oligodendrocytes have the machinery to assemble the myelin proteins and attach the sugars to them. *Id.* They lie next to the axons and produce the myelin that insulates them. *Id.* When the antibody attacks the oligodendrocytes, the reaction can get so viscous in the brain that it actually severs the axons. *Id.* This produces transected wires that are not going to grow back, leading to the progressive form of MS. *Id.* Dr. Steinman opined that Ms. Smith initially had relapsing–remitting MS, and then advanced to secondary progressive MS consistent with this explanation. *Id.* at 124.

Dr. Alexander did not dispute that molecular mimicry was a valid scientific theory, but he did not think that it applied to explain this case. He cited to the Ascherio study[9] which looked at the epidemiological correlation between the Hepatitis B vaccine and MS in a large cohort of nurses. Tr. at 224-26; *see generally* Pet. Ex. 54. The study found no epidemiological correlation or elevation in the rate of MS in these nurses in conjunction with receipt of this vaccine. Pet. Ex. 54 at 7. While this study certainly raises a question about the correlation proposed by Dr. Steinman, it is recognized that in this Program the claims involved are rare events and rare events are generally not well documented by epidemiology. *See Knudsen v. Sec'y of HHS*, 35 F.3d 543, 550 (Fed. Cir. 1994) (finding as irrelevant to causation the evidence of more occurrences of encephalopathies caused by a viral infection than encephalopathies caused by the DTP vaccine; and further noting that "[t]he bare statistical fact that there are more reported cases of viral encephalopathies than there are reported cases of DTP encephalopathies is not evidence that in a particular case an encephalopathy following a DTP vaccination was in fact caused by a viral infection present in the child and not caused by the DTP vaccine.").

The Federal Circuit has held that the petitioner's burden is to show that it is more likely than not that a disease was caused by a vaccine "in a field bereft of complete and direct proof of how vaccines affect the human body." *Althen v. Sec'y of HHS*, 418 F.3d 1274, 1280 (Fed. Cir. 2005). In *Capizzano*, the Federal Circuit stated: "we conclude that requiring either

[9] Pet. Ex. 54 (Ascherio A, Zhang SM, Hernan MA, et al., *Hepatitis B Vaccination and the Risk of Multiple Sclerosis*, 344 NEW ENGLAND J. OF MEDICINE 327-32 (2001).).

epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect is contrary to what we said in *Althen . . . .*" *Capizzano v. Sec'y of HHS*, 440 F.3d 1317, 1325 (Fed. Cir. 2006). "Requiring 'epidemiological studies . . . or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant's burden under the Vaccine Act and hinders the system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants.'" *Andreu*, 569 F.3d at 1378 (quoting *Capizzano*, 440 F.3d at 1325-26).

The issue of a causal connection between the Hepatitis B vaccine and demyelinating diseases, including multiple sclerosis, has been extensively litigated in this Program in an omnibus proceeding. Special Master Millman heard extensive evidence, as well as considered both the Bogdanos and Ascherio articles, in four paradigm cases in which she found that the Hepatitis B vaccine could cause transverse myelitis in *Stevens v. Sec'y of HHS*, No. 99-597, 2006 WL 659625, at *25 (Fed. Cl. Spec. Mstr. Feb. 24, 2006), that it could cause Guillain-Barré Syndrome and CIDP in *Gilbert v. Sec'y of HHS*, No. 04-455, 2006 WL 1006612, at *12 (Fed. Cl. Spec. Mstr. Mar. 30, 2006), and most relevant to this case, that it could cause multiple sclerosis in *Werderitsh v. Sec'y of HHS*, No. 99-310, 2006 WL 1672884, at *27 (Fed. Cl. Spec. Mstr. May 26, 2006). Much like in this case, there was considerable debate in the *Werderitsh* case about the date of onset. The respondent's experts contended that various symptoms going back ten years may have been caused by MS, whereas the petitioner's expert argued that visual symptoms occurring days to a week after the second vaccination was either the onset or represented a rechallenge phenomenon. *Werderitsh*, 2006 WL 1672884, at *15-22. Similarly in this case, Ms. Smith testified that she had transient visual spots when exposed to hot water in the shower after the second vaccination, but after the third in December 2006, the symptoms became much more pronounced and advanced to include not only abundant spots, but also episodic diplopia, and blurry vision. Special Master Millman extensively reviewed the literature submitted, much of which was submitted in this case as well, and concluded that in people who are genetically susceptible, an environmental trigger, which could be a vaccine, causes the body to attack itself causing lesions in the brain and spine separated in space and time. *Id.* at *24.

Also in *Fisher v. Sec'y of HHS*, No. 99-432, 2009 WL2365459, *3-7 (Fed. Cl. Spec. Mstr. July 23, 2009), Special Master Millman considered a case of a woman who made multiple visits to doctors with back pain and isolated numbness attributed to motor vehicle accidents and degenerative disc disease which were not diagnosed by her doctors as MS. Some months after receipt of the Hepatitis B vaccine, she had visual symptoms in addition to pain and transient left leg weakness, which was followed by subtle MRI findings consistent with MS. *Id.* The Special Master concluded after reviewing abundant literature and the testimony of respondent's expert that the petitioner had satisfied her burden of proof and was entitled to compensation based upon either a new onset or aggravation theory.[10] *Id.* at *16-20.

[10] Special Master Millman also decided other cases involving the Hepatitis B vaccine and multiple sclerosis in which the parties disputed the date of onset of the disease. In each case she decided that whether the vaccine caused new onset disease or an aggravation, the end result was the same and the petitioner was entitled to compensation. *See e.g.*, *Adler v. Sec'y of HHS*, No.

Although ten years has passed since the evidence was presented in that case, the medical understanding of causation in MS appears to be at a similar level today. As Dr. Steinman said, molecular mimicry provides a solid scientific foundation to explain the causation of MS, while acknowledging that the cause is still not well understood. Tr. at 74. Dr. Alexander relied primarily upon the Ascherio study as his basis for contending that it was unlikely that the Hepatitis B vaccine could cause MS. *Id.* at 224-26. However, as the Federal Circuit in *Capizzano* noted, epidemiological evidence is not required to establish the first prong of *Althen*. *Capizzano*, 440 F.3d at 1325.

I have concluded that Dr. Steinman presented a scientifically reasonable theory to explain how the Hepatitis B vaccine can act as the environmental trigger of MS through the mechanism of molecular mimicry, particularly with the myelin oligodendrocyte protein, and has accordingly established the first prong of *Althen* by a preponderance of the evidence.

3. *Althen* Prong Two

This is a case in which the theory proposed in *Althen* prong one and the logical explanation required for *Althen* prong two fit closely together. If it is accepted that molecular mimicry between the Hepatitis B vaccine could cause demyelination in the central nervous system by causing the immune system to mistake MOG for a foreign invader, as I have concluded, then the process by which it did so can be logically explained by a gradual increase in symptoms consistent with MS, including visual disturbances, dizziness, and fatigue which became progressively worse and went on to cause the secondarily progressive form of the disease. The conclusion of onset within the months following the third vaccination is also supported by the appearance of an enhancing lesion in the brain in May 2006. No prior MS lesions were seen on any of her MRIs. More numerous lesions appeared in subsequent MRIs. As such, the progression of Ms. Smith's disease can be logically explained as a process that was instigated by the vaccine as described by Dr. Steinman. No other explanation for an environmental trigger appears in the evidence, and accordingly, it is reasonable to conclude that the vaccine provided the necessary environmental trigger to cause the onset of MS such that she now has the progressive form of the disease with a great many lesions and chronic debilitating symptoms. She has established *Althen* prong two.

4. *Althen* Prong Three

Dr. Steinman testified that whether the initial symptoms of the disease occurred with the significant symptoms and events described by Kaitlyn and her mother on Christmas day 2005 or whether they developed over the three months preceding May 1, 2006 as reported in the medical records, the timing for the onset of the disease was appropriately related to the receipt of the third Hepatitis B vaccine on December 20, 2005. Tr. at 108-09. The onset would be dated within approximately four days to forty-two days (to approximately February 1, 2006), which has been

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99-608, 2008 WL 5068931, at *18 (Fed. Cl. Spec. Mstr. Nov. 18, 2008). These cases are not controlling, but I find them informative and persuasive.

accepted as a reasonable time for the onset of an adaptive autoimmune response triggered by a vaccine. *See id.* (discussing the swine flu and Guillain-Barré Syndrome study by Schonberger, submitted as petitioner's exhibit 51). I have concluded that, consistent with Dr. Steinman's unopposed testimony on this point, and findings in other cases, as cited above, that this is a reasonable time frame for the causation of the disease onset through the mechanism of molecular mimicry between the Hepatitis B vaccine and myelin oligodendrocyte protein or MOG.

III. CONCLUSION

Accordingly, I have concluded that the petitioner is entitled to compensation based upon the theory of molecular mimicry between the vaccine and the MOG component of myelin, with a date of onset of petitioner's multiple sclerosis occurring within four to approximately forty-two days after the receipt of the vaccination.

A separate damages order will be issued.

IT IS SO ORDERED.

s/ Thomas L. Gowen
Thomas L. Gowen
Special Master